

WEST Search History

DATE: Tuesday, August 15, 2006

<u>Hide?</u>	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
	<i>DB=PGPB,USPT,EPAB; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L46	L45 not @py>2001	3
<input type="checkbox"/>	L45	L29 and L7	33
<input type="checkbox"/>	L44	L29 and L27	0
<input type="checkbox"/>	L43	5955432.pn.	1
<input type="checkbox"/>	L42	5767086.pn.	1
<input type="checkbox"/>	L41	L40 not @py>2001	52
<input type="checkbox"/>	L40	L39 not @ay>2001	97
<input type="checkbox"/>	L39	L38 and L7	219
<input type="checkbox"/>	L38	glutathione SAME prodrug	252
<input type="checkbox"/>	L37	TER and glutathione	1042
<input type="checkbox"/>	L36	L35 and glutathione	19
<input type="checkbox"/>	L35	L34 not @ay>2001	31
<input type="checkbox"/>	L34	L33 and carboplatin	98
<input type="checkbox"/>	L33	L32 and L7	573
<input type="checkbox"/>	L32	TER and prodrug	787
<input type="checkbox"/>	L31	L30 not @ay>2001	3
<input type="checkbox"/>	L30	L29 and carboplatin	24
<input type="checkbox"/>	L29	TER286 or (TER-286) or (TER 286)	33
<input type="checkbox"/>	L28	5880097.pn.	1
<input type="checkbox"/>	L27	L4 and L7	1
<input type="checkbox"/>	L26	L7 and L11	1
<input type="checkbox"/>	L25	L24 and L3	8
<input type="checkbox"/>	L24	L23 and L7	132
<input type="checkbox"/>	L23	L22 and L14	157
<input type="checkbox"/>	L22	L21 or L20	3792
<input type="checkbox"/>	L21	(530/331 530/345)! [CCLS]	2582
<input type="checkbox"/>	L20	(514/18)! [CCLS]	2139
<input type="checkbox"/>	L19	L18 and L16	55
<input type="checkbox"/>	L18	L7.ab.	41561
<input type="checkbox"/>	L17	L16 and L7	133
<input type="checkbox"/>	L16	L15.ab.	264

<input type="checkbox"/>	L15	GST or (glutathione NEAR3 transferase)	25854
<input type="checkbox"/>	L14	GST or (glutathione NEAR2 transferase)	25839
<input type="checkbox"/>	L13	L12 and L7	58
<input type="checkbox"/>	L12	(ter NEAR2 286) or (TLK NEAR2 286)	58
<input type="checkbox"/>	L11	("5556942").PN.	1
<input type="checkbox"/>	L10	L9 not @py>2001	17
<input type="checkbox"/>	L9	L8 and L6	150
<input type="checkbox"/>	L8	L7.clm.	39760
<input type="checkbox"/>	L7	cancer\$ or neoplas\$ or tumor\$	196960
<input type="checkbox"/>	L6	L5.clm.	284
<input type="checkbox"/>	L5	combination therapy	16894
<input type="checkbox"/>	L4	5908919.pn.	1
<input type="checkbox"/>	L3	L2 or L1	58
<input type="checkbox"/>	L2	tlk 286	31
<input type="checkbox"/>	L1	ter 286	28

END OF SEARCH HISTORY

\$%^STN;HighlightOn= ***;HighlightOff=*** ;

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1642BJF

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

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STN Express with Discover!
NEWS 4 OCT 28 KOREAPAT now available on STN
NEWS 5 NOV 30 PHAR reloaded with additional data
NEWS 6 DEC 01 LISA now available on STN
NEWS 7 DEC 09 12 databases to be removed from STN on December 31, 2004
NEWS 8 DEC 15 MEDLINE update schedule for December 2004
NEWS 9 DEC 17 ELCOM reloaded; updating to resume; current-awareness
alerts (SDIs) affected
NEWS 10 DEC 17 COMPUAB reloaded; updating to resume; current-awareness
alerts (SDIs) affected
NEWS 11 DEC 17 SOLIDSTATE reloaded; updating to resume; current-awareness
alerts (SDIs) affected
NEWS 12 DEC 17 CERAB reloaded; updating to resume; current-awareness
alerts (SDIs) affected
NEWS 13 DEC 17 THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS 14 DEC 30 EPFULL: New patent full text database to be available on STN
NEWS 15 DEC 30 CAPLUS - PATENT COVERAGE EXPANDED
NEWS 16 JAN 03 No connect-hour charges in EPFULL during January and
February 2005
NEWS 17 FEB 25 CA/CAPLUS - Russian Agency for Patents and Trademarks
(ROSPATENT) added to list of core patent offices covered
NEWS 18 FEB 10 STN Patent Forums to be held in March 2005
NEWS 19 FEB 16 STN User Update to be held in conjunction with the 229th ACS
National Meeting on March 13, 2005
NEWS 20 FEB 28 PATDPAFULL - New display fields provide for legal status
data from INPADOC
NEWS 21 FEB 28 BABS - Current-awareness alerts (SDIs) available
NEWS 22 FEB 28 MEDLINE/LMEDLINE reloaded
NEWS 23 MAR 02 GBFULL: New full-text patent database on STN
NEWS 24 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS 25 MAR 03 MEDLINE file segment of TOXCENTER reloaded
NEWS 26 MAR 22 KOREAPAT now updated monthly; patent information enhanced
NEWS 27 MAR 22 Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS 28 MAR 22 PATDPASPC - New patent database available
NEWS 29 MAR 22 REGISTRY/ZREGISTRY enhanced with experimental property ta

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRI
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
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NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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***** STN Columbus *****

FILE 'HOME' ENTERED AT 10:35:18 ON 25 MAR 2005

=> file reg

COST IN U.S. DOLLARS	ENTRY	SINCE FILE SESSION	TOTAL
FULL ESTIMATED COST		0.21	0.21

FILE 'REGISTRY' ENTERED AT 10:35:27 ON 25 MAR 2005
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 24 MAR 2005 HIGHEST RN 847222-24-6
DICTIONARY FILE UPDATES: 24 MAR 2005 HIGHEST RN 847222-24-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> E "CANGLUSTRATIDE"/CN 25
E1 1 CANFOSFAMIDE/CN
E2 1 CANGITOXIN (REDUCED)/CN
E3 0 --> CANGLUSTRATIDE/CN
E4 1 CANGLUSTRATIDE HYDROCHLORIDE/CN
E5 1 CANGORIN A/CN
E6 1 CANGORIN B/CN
E7 1 CANGORIN C/CN
E8 1 CANGORIN D/CN
E9 1 CANGORIN E/CN
E10 1 CANGORIN F/CN
E11 1 CANGORIN G/CN
E12 1 CANGORIN H/CN
E13 1 CANGORIN I/CN
E14 1 CANGORIN J/CN
E15 1 CANGORINE A/CN
E16 1 CANGORINE B/CN
E17 1 CANGORINE C/CN
E18 1 CANGORINE D/CN
E19 1 CANGORINE E/CN
E20 1 CANGORINE F/CN
E21 1 CANGORINE G/CN
E22 1 CANGORINE G 10-ACETATE/CN
E23 1 CANGORINE H/CN
E24 1 CANGORINE I/CN
E25 1 CANGORINE J/CN

=> S E4
L1 1 "CANGLUSTRATIDE HYDROCHLORIDE"/CN

=> DIS L1 1 SQIDE
THE ESTIMATED COST FOR THIS REQUEST IS 6.15 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 439943-59-6 REGISTRY

CN Glycine, L-.gamma.-glutamyl-3-[[2-[[bis[bis(2-chloroethyl)amino]phosphinyl]oxy]ethyl]sulfonyl]-L-alanyl-2-phenyl-,
monohydrochloride, (2R)- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN ***Canglustratide hydrochloride***

CN TER 286

CN TLK 286

FS STEREOSEARCH

MF C26 H40 Cl4 N5 O10 P S . Cl H

SR CAS Client Services

LC STN Files: ADISINSIGHT, CA, CAPLUS, PHAR, PROUSDDR, SYNTHLINE,
TOXCENTER, USPATFULL

DT.CA Capius document type: Conference; Journal; Patent

RL.P Roles from patents: BIOL (Biological study); USES (Uses)

RLD.P Roles for non-specific derivatives from patents: BIOL (Biological
study); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); PROC (Process); USES
(Uses)

CRN (158382-37-7)

Absolute stereochemistry.

/ Structure 1 in file .gra /

18 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

18 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file medline

COST IN U.S. DOLLARS	ENTRY	SINCE FILE SESSION	TOTAL
FULL ESTIMATED COST		6.87	7.08

FILE 'MEDLINE' ENTERED AT 10:36:18 ON 25 MAR 2005

FILE LAST UPDATED: 24 MAR 2005 (20050324/UP). FILE COVERS 1950 TO DATE

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP
RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>

http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l1

L2 0 L1

=> file caplus

COST IN U.S. DOLLARS	ENTRY	SINCE FILE SESSION	TOTAL
FULL ESTIMATED COST		0.40	7.48

FILE 'CAPLUS' ENTERED AT 10:36:25 ON 25 MAR 2005

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FILE COVERS 1907 - 25 Mar 2005 VOL 142 ISS 14
FILE LAST UPDATED: 24 Mar 2005 (20050324/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l1
L3 18 L1

=> s l3 and (cancer? or tumor? or neoplas?)
253494 CANCER?
384869 TUMOR?
402446 NEOPLAS?
L4 18 L3 AND (CANCER? OR TUMOR? OR NEOPLAS?)

=> s l4 not py>2002
2461177 PY>2002
L5 8 L4 NOT PY>2002

=> d ibib 1-4

L5 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:61250 CAPLUS

DOCUMENT NUMBER: 139:143479

TITLE: Efficacy of a glutathione S-transferase .pi.-activated
prodrug in platinum-resistant ovarian ***cancer***
cells

AUTHOR(S): Townsend, Danyelle M.; Shen, Hongxie; Staros,
Alexandra L.; Gate, Laurent; Tew, Kenneth D.

CORPORATE SOURCE: Department of Pharmacology, Fox Chase Cancer Center
Philadelphia, PA, 19111, USA

SOURCE: Molecular Cancer Therapeutics (2002), 1(12), 1089-1095
CODEN: MCTOCF; ISSN: 1535-7163

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:316848 CAPLUS

DOCUMENT NUMBER: 135:116763

TITLE: The influence of GST-targeted drugs on cell
proliferation and stress response

AUTHOR(S): Tew, Kenneth D.

CORPORATE SOURCE: Department of Pharmacology, Fox Chase Cancer Center
Philadelphia, PA, USA

SOURCE: Chemico-Biological Interactions (2001), 133(1-3),
295-300
CODEN: CBINA8; ISSN: 0009-2797

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:466901 CAPLUS

DOCUMENT NUMBER: 133:171845

TITLE: Cellular response to a glutathione S-transferase P1-1
activated prodrug

AUTHOR(S): Rosario, Lilliam A.; O'Brien, Miechelle L.; Henderson,
Colin J.; Wolf, C. Roland; Tew, Kenneth D.

CORPORATE SOURCE: Department of Pharmacology, Fox Chase Cancer Center
Philadelphia, PA, USA
SOURCE: Molecular Pharmacology (2000), 58(1), 167-174
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental
Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:402062 CAPLUS

DOCUMENT NUMBER: 129:117526

TITLE: ***Tumor*** efficacy and bone marrow-sparing
properties of TER286, a cytotoxin activated by
glutathione S-transferase

AUTHOR(S): Morgan, Amy S.; Sanderson, Polly E.; Borch, Richard
F.; Tew, Kenneth D.; Niitsu, Yoshiro; Takayama,
Tetsuji; Von Hoff, Daniel D.; Izbicka, Elzbieta;
Mangold, Gina; Paul, Christer; Broberg, Ulrika;
Mannervik, Bengt; Henner, W. David; Kauvar, Lawrence
M.

CORPORATE SOURCE: Terrapin Technologies, Inc., South San Francisco, CA,
94080, USA

SOURCE: Cancer Research (1998), 58(12), 2568-2575

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 5-8

L5 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:348755 CAPLUS

DN 127:60274

TI Activity of TER286 against human ***tumor*** colony-forming units

AU Izbicka, Elzbieta; Lawrence, Richard; Cerna, Caesar; Von Hoff, Daniel D.;
Sanderson, Polly E.

CS Inst. Drug Development, Cancer Therapy Res. Center, San Antonio, TX,
78245, USA

SO Anti-Cancer Drugs (1997), 8(4), 345-348

CODEN: ANTDEV; ISSN: 0959-4973

PB Rapid Science Publishers

DT Journal

LA English

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECOR
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:695835 CAPLUS

DN 126:554

TI Glutathione-based anti- ***cancer*** drugs: Animal efficacy and bone
marrow sparing effects

AU Lyttle, M. H.; Satyam, A.; Hocker, M. D.; Hui, H. C.; Caldwell, C. G.;
Morgan, A. S.; Stanboli, A.; Kauvar, L. M.

CS Terrapin Technologies, South San Francisco, CA, 94080, USA

SO Peptides: Chemistry, Structure and Biology, Proceedings of the American
Peptide Symposium, 14th, Columbus, Ohio, June 18-23, 1995 (1996), Meeting
Date 1995, 170-171. Editor(s): Kaumaya, Pravin T. P.; Hodges, Robert S.
Publisher: Mayflower Scientific, Kingswinford, UK.
CODEN: 63NTAF

DT Conference

LA English

L5 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:175896 CAPLUS

DN 124:278186

TI Design, Synthesis, and Evaluation of Latent Alkylating Agents Activated by
Glutathione S-Transferase

AU Satyam, Apparao; Hocker, Michael D.; Kane-Maguire, Kim A.; Morgan, Amy S.;

Villar, Hugo O.; Lyttle, Matthew H.
CS Terrapin Technologies Inc., South San Francisco, CA, 94080, USA
SO Journal of Medicinal Chemistry (1996), 39(8), 1736-47
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English

L5 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:892014 CAPLUS
DN 124:21231

TI Modulation of detoxification gene expression in human colon HT29 cells by
glutathione-S-transferase inhibitors

AU Ciaccio, Paul J.; Shen, Hongxie; Jaiswal, Anil K.; Lyttle, Matthew H.;
Tew, Kenneth D.

CS Dep. Pharmacol., Fox Chase Cancer Cent., Philadelphia, PA, 19111, USA

SO Molecular Pharmacology (1995), 48(4), 639-47

CODEN: MOPMA3; ISSN: 0026-895X

PB Williams & Wilkins

DT Journal

LA English

=> file pctfull

COST IN U.S. DOLLARS	ENTRY	SINCE FILE SESSION	TOTAL
FULL ESTIMATED COST		17.71	25.19

FILE 'PCTFULL' ENTERED AT 10:38:07 ON 25 MAR 2005
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FILE LAST UPDATED: 23 MAR 2005 <20050323/UP>
MOST RECENT UPDATE WEEK: 200511 <200511/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

=> s l1

'CN' IS NOT A VALID FIELD CODE

L6 0 "CANGLUSTRATIDE HYDROCHLORIDE"/CN

=> s canglustratide

L7 1 CANGLUSTRATIDE

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	ENTRY	SINCE FILE SESSION	TOTAL
FULL ESTIMATED COST		1.05	26.24

STN INTERNATIONAL LOGOFF AT 10:38:43 ON 25 MAR 2005

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NEWS 3 FEB 27 New STN AnaVist pricing effective March 1, 2006
NEWS 4 APR 04 STN AnaVist \$500 visualization usage credit offered
NEWS 5 MAY 10 CA/CaPlus enhanced with 1900-1906 U.S. patent records
NEWS 6 MAY 11 KOREAPAT updates resume
NEWS 7 MAY 19 Derwent World Patents Index to be reloaded and enhanced
NEWS 8 MAY 30 IPC 8 Rolled-up Core codes added to CA/CaPlus and
USPATFULL/USPAT2
NEWS 9 MAY 30 The F-Term thesaurus is now available in CA/CaPlus
NEWS 10 JUN 02 The first reclassification of IPC codes now complete in
INPADOC
NEWS 11 JUN 26 TULSA/TULSA2 reloaded and enhanced with new search and
and display fields
NEWS 12 JUN 28 Price changes in full-text patent databases EPFULL and PCTFULL
NEWS 13 JUL 11 CHEMSAFE reloaded and enhanced
NEWS 14 JUL 14 FSTA enhanced with Japanese patents
NEWS 15 JUL 19 Coverage of Research Disclosure reinstated in DWPI
NEWS 16 AUG 09 INSPEC enhanced with 1898-1968 archive

NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
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NEWS IPC8 For general information regarding STN implementation of IPC 8
NEWS X25 X.25 communication option no longer available

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FILE 'HOME' ENTERED AT 09:33:34 ON 14 AUG 2006

=> file caplus			
COST IN U.S. DOLLARS		SINCE FILE	TOTAL
	ENTRY	SESSION	
FULL ESTIMATED COST		0.21	0.21

FILE 'CAPLUS' ENTERED AT 09:33:41 ON 14 AUG 2006
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FILE COVERS 1907 - 14 Aug 2006 VOL 145 ISS 8
FILE LAST UPDATED: 13 Aug 2006 (20060813/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

=> s 439943-59-6/rn
31 439943-59-6
2 439943-59-6D
L1 29 439943-59-6/RN
(439943-59-6 (NOTL) 439943-59-6D)

=> s carboplatin/cn
*** REG1stRY INITIATED ***

Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L3 4320 L2

=> s l1 and l3
L4 11 L1 AND L3

=> d ibib 1-11

L4 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:167588 CAPLUS <<LOGINID::20060814>>
DOCUMENT NUMBER: 144:254148
TITLE: Aminopteridinones as anticancer agents, their
preparation, pharmaceutical compositions, and use in
therapy
INVENTOR(S): Munzert, Gerd; Steegmaier, Martin; Baum, Anke
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany;
Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006018182	A1	20060223	WO 2005-EP8623	20050809
WO 2006018182	C1	20060608		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006058311	A1	20060316	US 2005-189540	20050726
PRIORITY APPLN. INFO.: EP 2004-19361 A 20040814				
EP 2004-19448 A 20040817				
OTHER SOURCE(S): MARPAT 144:254148				
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT				

L4 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1290072 CAPLUS <<LOGINID::20060814>>
DOCUMENT NUMBER: 144:46998
TITLE: The X-ray crystal structure of BRCA1 tandem BRCT repeat and BACH1 phosphopeptide complex and methods and compositions for antitumor drug design
INVENTOR(S): Yaffe, Michael B.; Clapperton, Julie A.; Manke, Isaac A.; Lowery, Drew M.; Ho, Timmy; Haire, Lesley F.; Smerdon, Stephen J.

PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 360 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005115454	A2	20051208	WO 2005-US15981	20050509
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2004-569131P P 20040507

L4 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1242685 CAPLUS <<LOGINID::20060814>>
DOCUMENT NUMBER: 143:472533
TITLE: GST-activated anticancer therapy for sensitization or side effect amelioration of another anticancer
INVENTOR(S): Brown, Gail L.; Keck, James G.; Wick, Michael M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 13 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005261202	A1	20051124	US 2005-133833	20050519
WO 2005112973	A1	20051201	WO 2005-US17960	20050519
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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PRIORITY APPLN. INFO.: US 2004-572790P P 20040520
OTHER SOURCE(S): MARPAT 143:472533

L4 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1239173 CAPLUS <<LOGINID::20060814>>
DOCUMENT NUMBER: 143:477963
TITLE: Preparation of pyrazolyl urea derivatives as TrkA kinase inhibitors useful in the treatment of cancer
INVENTOR(S): Lee, Wendy; Ladouceur, Gaetan; Dumas, Jacques; Smith, Roger; Ying, Shihong; Wang, Gan; Chen, Zhi; Liu, Qingjie; Mokdad, Holia Hatoum
PATENT ASSIGNEE(S): Bayer Pharmacueticals Corporation, USA
SOURCE: PCT Int. Appl., 215 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110994	A2	20051124	WO 2005-US15106	20050502
WO 2005110994	A3	20060202		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-566445P P 20040430
OTHER SOURCE(S): MARPAT 143:477963

L4 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:409543 CAPLUS <<LOGINID::20060814>>
DOCUMENT NUMBER: 142:457053
TITLE: Human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy

INVENTOR(S): Lacasse, Eric; McManus, Daniel
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042558	A1	20050512	WO 2004-CA1902	20041029

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005148535	A1	20050707	US 2004-975974	20041028
CA 2542904	AA	20050512	CA 2004-2542904	20041029
EP 1682565	A1	20060726	EP 2004-789809	20041029

R: DE, FR, GB

PRIORITY APPLN. INFO.: US 2003-516192P P 20031030
WO 2004-CA1902 W 20041029

L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:409357 CAPLUS <<LOGINID::20060814>>
DOCUMENT NUMBER: 142:457052
TITLE: Sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with a chemotherapeutic agent

INVENTOR(S): Lacasse, Eric; McManus, Daniel; Durkin, Jon P.
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042030	A1	20050512	WO 2004-CA1900	20041029

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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US 2005119217 A1 20050602 US 2004-975790 20041028
AU 2004284855 A1 20050512 AU 2004-284855 20041029
CA 2542884 AA 20050512 CA 2004-2542884 20041029
PRIORITY APPLN. INFO.: US 2003-516263P P 20031030
WO 2004-CA1900 W 20041029

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:283298 CAPLUS <<LOGINID::20060814>>
DOCUMENT NUMBER: 142:349042
TITLE: Combinations of chlorpromazine compounds and
antiproliferative drugs for the treatment of neoplasms
INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen;
Keith, Curtis
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027842	A2	20050331	WO 2004-US30368	20040916
WO 2005027842	A3	20051222		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004273910	A1	20050331	AU 2004-273910	20040916
CA 2538570	AA	20050331	CA 2004-2538570	20040916
EP 1670477	A2	20060621	EP 2004-788798	20040916

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
PRIORITY APPLN. INFO.: US 2003-504310P P 20030918
WO 2004-US30368 W 20040916
OTHER SOURCE(S): MARPAT 142:349042

L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:158629 CAPLUS <<LOGINID::20060814>>
DOCUMENT NUMBER: 142:246160
TITLE: Treatment of lung cancer with vitamin D compounds in
combination with other treatments
INVENTOR(S): Henner, William D.
PATENT ASSIGNEE(S): Novacea, Inc., USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005016872 A1 20050224 WO 2004-US18427 20040610
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
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NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
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SN, TD, TG
AU 2004265238 A1 20050224 AU 2004-265238 20040610
CA 2528519 AA 20050224 CA 2004-2528519 20040610
EP 1631543 A1 20060308 EP 2004-776421 20040610
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK
CN 1802349 A 20060712 CN 2004-80015998 20040610
US 2006172014 A1 20060803 US 2005-298927 20051212
PRIORITY APPLN. INFO.: US 2003-477339P P 20030611
US 2004-569245P P 20040510
WO 2004-US18427 W 20040610
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:965067 CAPLUS <<LOGINID::20060814>>
DOCUMENT NUMBER: 141:406039
TITLE: Combinations for the treatment of diseases involving
cell proliferation, migration or apoptosis of myeloma
cells, or angiogenesis
INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin
Friedrich; Baum, Anke; Munzert, Gerd; Van Meel,
Jacobus C. A.
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany;
Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096224	A2	20041111	WO 2004-EP4363	20040424
WO 2004096224	A3	20041216		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1473043	A1	20041103	EP 2003-9587	20030429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004233576	A1	20041111	AU 2004-233576	20040424
CA 2523868	AA	20041111	CA 2004-2523868	20040424
EP 1622619	A2	20060208	EP 2004-729366	20040424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004009919	A	20060425	BR 2004-9919	20040424
NO 2005005605	A	20051128	NO 2005-5605	20051128
PRIORITY APPLN. INFO.: EP 2003-9587 A 20030429 EP 2004-508 A 20040113 EP 2004-1171 A 20040121 WO 2004-EP4363 W 20040424				

ACCESSION NUMBER: 2004:756710 CAPLUS <<LOGINID::20060814>>
 DOCUMENT NUMBER: 141:277628
 TITLE: Preparation of ureidophenoxycyanopyridines as anticancer drugs.
 INVENTOR(S): Scott, William J.; Dumas, Jacques; Boyer, Stephen; Lee, Wendy; Chen, Yuanwei; Phillips, Barton; Verma, Sharad; Chen, Jianqing; Chen, Zhi; Fan, Jianmei; Raudenbush, Brian; Redman, Aniko; Yi, Lin; Zhu, Qingming
 PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
 SOURCE: PCT Int. Appl., 127 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078747	A1	20040916	WO 2004-US6286	20040301
WO 2004078747	C1	20041104		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004235829	A1	20041125	US 2004-788029	20040227
AU 2004217977	A1	20040916	AU 2004-217977	20040301
CA 2517361	AA	20040916	CA 2004-2517361	20040301
US 2004229937	A1	20041118	US 2004-789446	20040301
US 2005032798	A1	20050210	US 2004-788405	20040301
US 2005038031	A1	20050217	US 2004-788426	20040301
EP 1599467	A1	20051130	EP 2004-716144	20040301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK BR 2004007897 A 20060301 BR 2004-7897 20040301				
PRIORITY APPLN. INFO.: US 2003-450323P P 20030228 US 2003-450324P P 20030228 US 2003-450348P P 20030228 WO 2004-US6286 A 20040301				
OTHER SOURCE(S): MARPAT 141:277628 REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT				

L4 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:453016 CAPLUS <<LOGINID::20060814>>
 DOCUMENT NUMBER: 141:1227
 TITLE: Combination cancer therapy with a glutathione S-transferase (GST)-activated anticancer compound and another anticancer therapy
 INVENTOR(S): Xu, Hua; Brown, Gail L.; Schow, Steven R.; Keck, James G.
 PATENT ASSIGNEE(S): Telik, Inc., USA
 SOURCE: PCT Int. Appl., 38 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004045593	A2	20040603	WO 2003-US36209	20031114
WO 2004045593	A3	20040812		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,				

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 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2505377 AA 20040603 CA 2003-2505377 20031114
 AU 2003290805 A1 20040615 AU 2003-290805 20031114
 US 2004138140 A1 20040715 US 2003-714593 20031114
 EP 1562564 A2 20050817 EP 2003-783388 20031114
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 BR 2003016364 A 20051004 BR 2003-16364 20031114
 CN 1711076 A 20051221 CN 2003-80103404 20031114
 JP 2006508980 T2 20060316 JP 2004-553614 20031114
 PRIORITY APPLN. INFO.: US 2002-426983P P 20021115
 WO 2003-US36209 W 20031114
 OTHER SOURCE(S): MARPAT 141:1227

=> s combination
 0 COMBINATINATION
 L5 0 COMBINATINATION

=> s combination
 470601 COMBINATION
 110564 COMBINATIONS
 L6 557159 COMBINATION
 (COMBINATION OR COMBINATIONS)

=> s l6 and l1
 L7 16 L6 AND L1

=> s l7 not py>2002
 4187833 PY>2002
 L8 2 L7 NOT PY>2002

=> d ibib 1-2

L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2001:316848 CAPLUS <<LOGINID::20060814>>
 DOCUMENT NUMBER: 135:116763
 TITLE: The influence of GST-targeted drugs on cell
 proliferation and stress response
 AUTHOR(S): Tew, Kenneth D.
 CORPORATE SOURCE: Department of Pharmacology, Fox Chase Cancer Center
 Philadelphia, PA, USA
 SOURCE: Chemico-Biological Interactions (2001), 133(1-3),
 295-300
 CODEN: CBINA8; ISSN: 0009-2797
 PUBLISHER: Elsevier Science Ireland Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2000:466901 CAPLUS <<LOGINID::20060814>>
 DOCUMENT NUMBER: 133:171845
 TITLE: Cellular response to a glutathione S-transferase P1-1
 activated prodrug
 AUTHOR(S): Rosario, Lilliam A.; O'Brien, Michelle L.; Henderson,
 Colin J.; Wolf, C. Roland; Tew, Kenneth D.
 CORPORATE SOURCE: Department of Pharmacology, Fox Chase Cancer Center
 Philadelphia, PA, USA
 SOURCE: Molecular Pharmacology (2000), 58(1), 167-174
 CODEN: MOPMA3; ISSN: 0026-895X
 PUBLISHER: American Society for Pharmacology and Experimental
 Therapeutics
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs kwic 1-2

L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:316848 CAPLUS <<LOGINID::20060814>>

DOCUMENT NUMBER: 135:116763

TITLE: The influence of GST-targeted drugs on cell proliferation and stress response

AUTHOR(S): Tew, Kenneth D.

CORPORATE SOURCE: Department of Pharmacology, Fox Chase Cancer Center
Philadelphia, PA, USA

SOURCE: Chemico-Biological Interactions (2001), 133(1-3),
295-300

CODEN: CBINA8; ISSN: 0009-2797

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Novel approaches to target GSTP-1 have produced two new anticancer drugs.

A GSTP1-1 activated nitrogen mustard prodrug (TER286) is selectively cytotoxic to tumors, which express high levels of the isoenzyme. Cells transfected with GSTP1-1 are more sensitive to the drug and resistant cells down regulate GSTP1-1 expression. A peptidomimetic inhibitor of GSTP1-1 (TER199) which modulates drug resistance when given in ***combination*** with either alkylating agents or natural products also ameliorated drug-induced bone marrow suppressive effects and possessed myeloproliferative activity. This effect is consistent with drug induced dissoch. of GSTP1-1 from JNK with resultant downstream proliferative effects.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Novel approaches to target GSTP-1 have produced two new anticancer drugs.

A GSTP1-1 activated nitrogen mustard prodrug (TER286) is selectively cytotoxic to tumors, which express high levels of the isoenzyme. Cells transfected with GSTP1-1 are more sensitive to the drug and resistant cells down regulate GSTP1-1 expression. A peptidomimetic inhibitor of GSTP1-1 (TER199) which modulates drug resistance when given in ***combination*** with either alkylating agents or natural products also ameliorated drug-induced bone marrow suppressive effects and possessed myeloproliferative activity. This effect is consistent with drug induced dissoch. of GSTP1-1 from JNK with resultant downstream proliferative effects.

IT 148-82-3, Melphalan 15663-27-1, Cisplatin 25316-40-9, Adriamycin 33069-62-4, Taxol 168682-53-9, TER199 ***439943-59-6***, TER 286
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(influence of glutathione S-transferase-targeted anticancer drugs on cell proliferation and stress response)

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:466901 CAPLUS <<LOGINID::20060814>>

DOCUMENT NUMBER: 133:171845

TITLE: Cellular response to a glutathione S-transferase P1-1 activated prodrug

AUTHOR(S): Rosario, Lilliam A.; O'Brien, Michelle L.; Henderson, Colin J.; Wolf, C. Roland; Tew, Kenneth D.

CORPORATE SOURCE: Department of Pharmacology, Fox Chase Cancer Center
Philadelphia, PA, USA

SOURCE: Molecular Pharmacology (2000), 58(1), 167-174

CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB TER286 [.gamma.-glutamyl-.alpha.-amino-.beta.(2-ethyl-N,N,N',N'-tetrakis(2-chloroethyl)phosphorodiamidate)-sulfonyl-propionyl-(R)-(-) phenylglycine] is a novel nitrogen mustard prodrug that is preferentially activated by glutathione S-transferase P1-1 (GSTP1-1). A human promyelocytic leukemia /TER286-resistant cell line was selected by chronic, long-term exposure to the prodrug. Although resistance was not readily achieved, eventually a 5-fold resistant clone was isolated. Cross-resistance to melphalan occurred, but not to doxorubicin (Adriamycin), taxol, and .gamma.-glutamyl-S-(benzyl)cysteinyl-R(-)-Ph glycine di-Et ester, a GSTP1-1 inhibitor. The protein and transcript levels and enzymic activity of GSTP1-1 were reduced significantly in the selected resistant line. GST.alpha. levels were unchanged, and GST.mu. was undetectable. Although glutathione levels were elevated in human promyelocytic leukemia/TER286

cells, no changes in the expression of thiol-related genes including .gamma.-glutamylcysteine synthetase, .gamma.-glutamyl transpeptidase, or multidrug resistance protein were found. A 7-fold increase in catalase expression in the resistant cell line indicated an adaptive response to oxidative and electrophilic stress, and this was also reflected in the lower prevalence of drug-induced DNA single-strand breaks in the resistant cells. Mouse embryo fibroblast GSTP1-1-/- cells exhibited 2-fold resistance to TER286 compared with GSTP1-1+/+ cells. NIH3T3 cells transfected with ***combinations*** of .gamma.-GCS and multidrug resistance protein exhibited enhanced resistance to TER286, although the degree of resistance was impaired by co-transfection of GSTP1-1. These results are consistent with responses in the TER286-resistant cells indicative of GSTP1-1-mediated mechanism of activation. In consequence, these data support the rationale that tumors expressing high levels of GSTP1-1 will be more sensitive to the cytotoxic effects of the drug.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB TER286 [.gamma.-glutamyl-.alpha.-amino-.beta.(2-ethyl-N,N,N',N'-tetrakis(2-chloroethyl)phosphorodiamidate)-sulfonyl-propionyl-(R)-(-) phenylglycine] is a novel nitrogen mustard prodrug that is preferentially activated by glutathione S-transferase P1-1 (GSTP1-1). A human promyelocytic leukemia /TER286-resistant cell line was selected by chronic, long-term exposure to the prodrug. Although resistance was not readily achieved, eventually a 5-fold resistant clone was isolated. Cross-resistance to melphalan occurred, but not to doxorubicin (Adriamycin), taxol, and .gamma.-glutamyl-S-(benzyl)cysteinyl-R(-)-Ph glycine di-Et ester, a GSTP1-1 inhibitor. The protein and transcript levels and enzymic activity of GSTP1-1 were reduced significantly in the selected resistant line. GST.alpha. levels were unchanged, and GST.mu. was undetectable. Although glutathione levels were elevated in human promyelocytic leukemia/TER286 cells, no changes in the expression of thiol-related genes including .gamma.-glutamylcysteine synthetase, .gamma.-glutamyl transpeptidase, or multidrug resistance protein were found. A 7-fold increase in catalase expression in the resistant cell line indicated an adaptive response to oxidative and electrophilic stress, and this was also reflected in the lower prevalence of drug-induced DNA single-strand breaks in the resistant cells. Mouse embryo fibroblast GSTP1-1-/- cells exhibited 2-fold resistance to TER286 compared with GSTP1-1+/+ cells. NIH3T3 cells transfected with ***combinations*** of .gamma.-GCS and multidrug resistance protein exhibited enhanced resistance to TER286, although the degree of resistance was impaired by co-transfection of GSTP1-1. These results are consistent with responses in the TER286-resistant cells indicative of GSTP1-1-mediated mechanism of activation. In consequence, these data support the rationale that tumors expressing high levels of GSTP1-1 will be more sensitive to the cytotoxic effects of the drug.

IT 148-82-3, Melphalan 23214-92-8, Doxorubicin ***439943-59-6*** , TER 286

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effect of exposure to a glutathione S-transferase P1-1 activated prodrug on antitumor agent resistance of human promyelocytic leukemia cell lines)

=> TER199/cn

TER199 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.

For a list of commands available to you in the current file, enter

"HELP COMMANDS" at an arrow prompt (=>).

=> s TER199/cn

*** REG1stRY INITIATED ***

Substance data SEARCH and crossover from CAS REGISTRY in progress...

Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

=> s TER 199/cn

*** REG1stRY INITIATED ***

Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L12 17 L11

=> s combined or combination

460593 COMBINED

470601 COMBINATION

110564 COMBINATIONS

557159 COMBINATION

(COMBINATION OR COMBINATIONS)

L13 965782 COMBINED OR COMBINATION

=> s l13 and l12

L14 4 L13 AND L12

=> d ibib 1-4

L14 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:683236 CAPLUS <<LOGINID::20060814>>

DOCUMENT NUMBER: 140:122233

TITLE: Reversal of multiple drug resistance in
cholangiocarcinoma by the glutathione
S-transferase-.pi.-specific inhibitor
O1-hexadecyl-.gamma.-glutamyl-S-benzylcysteinyI-D-
phenylglycine Ethylester

AUTHOR(S): Nakajima, Takaharu; Takayama, Tetsuji; Miyanishi,
Koji; Nobuoka, Atsushi; Hayashi, Tsuyoshi; Abe,
Tomoyuki; Kato, Junji; Sakon, Kiyoyuki; Naniwa,
Yoshimitsu; Tanabe, Hirohumi; Niitsu, Yoshiro

CORPORATE SOURCE: Fourth Department of Internal Medicine, Sapporo
Medical University School of Medicine, Sapporo, Japan

SOURCE: Journal of Pharmacology and Experimental Therapeutics
(2003), 306(3), 861-869

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental
Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:414079 CAPLUS <<LOGINID::20060814>>

DOCUMENT NUMBER: 138:406943

TITLE: Pharmaceutical compositions containing glutathione
analogs

INVENTOR(S): Kauvar, Lawrence M.; Lum, Robert T.; Lyttle, Matthew
H.; Macsata, Robert W.; Schow, Steven R.; Villar, Hugo
O.; Kozlowski, Michael R.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 16 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003100511	A1	20030529	US 2001-903442	20010710
US 7029695	B2	20060418		

PRIORITY APPLN. INFO.: US 2001-903442 20010710

OTHER SOURCE(S): MARPAT 138:406943

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:364945 CAPLUS <<LOGINID::20060814>>
 DOCUMENT NUMBER: 139:207702
 TITLE: Resistance to phorbol 12-myristate 13-acetate-induced
 cell growth arrest in an HL60 cell line chronically
 exposed to a glutathione S-transferase .pi. inhibitor
 AUTHOR(S): Gate, Laurent; Lunk, Alexandra; Tew, Kenneth D.
 CORPORATE SOURCE: Department of Pharmacology, Fox Chase Cancer Center
 Philadelphia, PA, 19111, USA
 SOURCE: Biochemical Pharmacology (2003), 65(10), 1611-1622
 CODEN: BCPA6; ISSN: 0006-2952
 PUBLISHER: Elsevier Science Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2001:316848 CAPLUS <<LOGINID::20060814>>
 DOCUMENT NUMBER: 135:116763
 TITLE: The influence of GST-targeted drugs on cell
 proliferation and stress response
 AUTHOR(S): Tew, Kenneth D.
 CORPORATE SOURCE: Department of Pharmacology, Fox Chase Cancer Center
 Philadelphia, PA, USA
 SOURCE: Chemico-Biological Interactions (2001), 133(1-3),
 295-300
 CODEN: CBINA8; ISSN: 0009-2797
 PUBLISHER: Elsevier Science Ireland Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE F
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d kwic 2

L14 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
 AB . . . hematopoiesis, protect hematopoietic cells from damage caused by
 radiation or chemotherapy, or potentiate the stimulatory action of one or
 a ***combination*** of cytokines on colony formation by hematopoietic
 progenitor cells, protect a subject from a destructive effect of a
 chemotherapeutic agent. . .
 IT ***168682-53-9P*** 286942-97-0P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (pharmaceutical compns. contg. glutathione analogs)

=> file pctfull

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 FILE COVERS 1978 TO DATE

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 SEE
<http://www.stn-international.de/stndatabases/details/ipc-reform.html> >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE

(last updated April 10, 2006) <<<

>>> NEW PRICES IN PCTFULL AS OF 01 JULY 2006. FOR DETAILS,
PLEASE SEE HELP COST <<<

=> s TER () (286 or 199)

64391 TER

9512 TERS

69137 TER

(TER OR TERS)

38923 286

65479 199

L15 15 TER (W) (286 OR 199)

=> s combination or combined

452833 COMBINATION

199923 COMBINATIONS

492208 COMBINATION

(COMBINATION OR COMBINATIONS)

331462 COMBINED

3 COMBINEDS

331463 COMBINED

(COMBINED OR COMBINEDS)

L16 564675 COMBINATION OR COMBINED

=> s l15 and l16

L17 14 L15 AND L16

=> s l17 not py>2001

533324 PY>2001

L18 5 L17 NOT PY>2001

=> d ibib 1-5

L18 ANSWER 1 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999037802 PCTFULL ED 20020515 <<LOGINID::2006C

TITLE (ENGLISH): METHODS TO IDENTIFY MYELOSTIMULANTS

TITLE (FRENCH): METHODES D'IDENTIFICATION DE MYELOSTIMULANTS

INVENTOR(S): KAUVAR, Lawrence, M.

PATENT ASSIGNEE(S): TELIK, INC.

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
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WO 9937802	A1	19990729
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DESIGNATED STATES

W: AU CA GD IN JP AT BE CH CY DE DK ES FI FR GB GR IE IT

LU MC NL PT SE

APPLICATION INFO.: WO 1999-US765 A 19990114

PRIORITY INFO.: US 1998-09/010,390 19980121

L18 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER: 1997025342 PCTFULL ED 20020514 <<LOGINID::2006C

TITLE (ENGLISH): TETHERED PRODRUGS BY VIRTUE OF COVALENT LINKAGE
ANALOGS OF GLUTATHIONE

TITLE (FRENCH): PRECURSEURS DE MEDICAMENTS LIES PAR UNE LIAISON
COVALENTE A L'AIDE D'ANALOGUES DE GLUTATHIONE

INVENTOR(S): LYTTLE, Matthew, H.;

KAUVAR, Lawrence, M.

PATENT ASSIGNEE(S): TERRAPIN TECHNOLOGIES, INC.

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
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WO 9725342	A1	19970717
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DESIGNATED STATES

W: AU CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL

PT SE

APPLICATION INFO.: WO 1996-US20042 A 19961220

PRIORITY INFO.: US 1996-8/582,966 19960104

L18 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER: 1996040205 PCTFULL ED 20020514 <<LOGINID::2006C
 TITLE (ENGLISH): METABOLIC EFFECTS OF CERTAIN GLUTATHIONE ANALO
 TITLE (FRENCH): EFFETS METABOLIQUES DE CERTAINS ANALOGUES DE
 GLUTATHIONE
 INVENTOR(S): KAUVAR, Lawrence, M.;
 LYTTLE, Matthew, H.;
 MORGAN, Amy, S.;
 BORCH, Richard, F.
 PATENT ASSIGNEE(S): TERRAPIN TECHNOLOGIES, INC.
 LANGUAGE OF PUBL.: English
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9640205	A1	19961219

 DESIGNATED STATES
 W: AL AM AU BB BG BR CA CN CZ EE GE HU IL IS JP KG KP KR
 LK LR LT LV MD MG MK MN MX NO NZ PL RO SG SI SK TR TT
 UA UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM
 AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF
 BJ CF CG CI CM GA GN ML MR NE SN TD TG
 APPLICATION INFO.: WO 1996-US9057 A 19960605
 PRIORITY INFO.: US 1995-8/482,645 19950607
 US 1996-8/636,516 19960419

L18 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
 ACCESSION NUMBER: 1995009866 PCTFULL ED 20020514 <<LOGINID::2006C
 TITLE (ENGLISH): GLUTATHIONE S-TRANSFERASE-ACTIVATED COMPOUND
 TITLE (FRENCH): COMPOSES ACTIVES PAR LA GLUTATHIONE S-TRANSFEE
 INVENTOR(S): KAUVAR, Lawrence, M.;
 LYTTLE, Matthew, H.;
 SATYAM, Apparao
 PATENT ASSIGNEE(S): TERRAPIN TECHNOLOGIES, INC.
 LANGUAGE OF PUBL.: English
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9509866	A1	19950413

 DESIGNATED STATES
 W: AU CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT
 SE
 APPLICATION INFO.: WO 1994-US11109 A 19940930
 PRIORITY INFO.: US 1993-8/130,736 19931001
 US 1994-8/309,005 19940919

L18 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
 ACCESSION NUMBER: 1995009865 PCTFULL ED 20020514 <<LOGINID::2006C
 TITLE (ENGLISH): GLUTATHIONE S-TRANSFERASE-ACTIVATED COMPOUND
 TITLE (FRENCH): COMPOSES ACTIVES PAR LA GLUTATHIONE S-TRANSFEE
 INVENTOR(S): KAUVAR, Lawrence, M.;
 LYTTLE, Matthew, H.;
 SATYAM, Apparao
 PATENT ASSIGNEE(S): TERRAPIN TECHNOLOGIES, INC.
 LANGUAGE OF PUBL.: English
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9509865	A1	19950413

 DESIGNATED STATES
 W: AU CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT
 SE
 APPLICATION INFO.: WO 1994-US10796 A 19940923
 PRIORITY INFO.: US 1993-8/130,736 19931001
 US 1994-8/130,736 19940919

=> d kwic 2-5

L18 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD However, TER 117 does not. A prodrug constructed from
 TER 117 as described in the above-referenced PCT

application, ***TER*** ***286***, has the desired isoenzyme specificity for cells having GST complements high in the P1-1 isoform; however, this form of the prodrug would.

or acid at a temperature of from about 0°C to about 100°C, preferably at room temperature either in water alone or in ***combination*** with an inert water-miscible organic solvent such as methanol, ethanol or dioxane.

in the PCT application, TER 231 is especially susceptible to cleavage by GST M1a-1a; TER 303 is especially susceptible to cleavage by A1-1; ***TER*** ***286*** is particularly susceptible to cleavage by P1-1 and A1-1, while TER 296 is selectively cleaved by P1. Thus, in treating a tumor having elevated levels of P1 use of a compound of formula (1) having the tripeptide contained in TER 296 or ***TER*** ***286*** would be preferred. The relevant isoenzyme, GST P1-1 is elevated in more than 75% of human tumor specimens from breast, lung, liver.

L18 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . toxic effect of TER199 in contrast to its unesterified form on HT4-1 cells, Figure 2 is a graph showing the effect of various ***combinations*** of chlorambucil either alone or in ***combination*** with ethacrynic acid or TER199.

in tumor cells. Third, the compounds of formula (1) directly potentiate the effect of chemotherapeutic agents in the destruction of tumor cells. This ***combination*** of qualities makes the compounds of the invention useful both as hematopoiesis potentiating agents directly and to ameliorate the negative effects of chemotherapeutic.

CMB, reducing the concentration CMB needed for 50% cell killing by a DMF of 1,08, In contrast the diethyl ester of 7E-C(Bz)-qG (***TER*** ***199***) at only 12.5 pM enhanced CMB cytotoxicity by a factor of 1. Preferential expression of GST isoenzyme P1-1 has been reported in a.

5 when TER199 was administered along with the melphalan, the tumor volume mean was approximately 55% of control. For group 4 administered a ***combination*** of melphalan and ethacrynic acid, the volumes were approximately 35% of control. Thus, both ethacrynic acid and TER199 potentiate the effects of.

GM-CSFI G-CSFI M-CSFI Flt3/Flk-2 and Steel factor (stem cell factor/c-kit ligand). Of particular interest was the finding that TER199 enhances colony formation stimulated by ***combinations*** of cytokines. Additionally, the enhancing effect is more pronounced in human than in murine bone marrow, These results suggest that TER199 has.

(60)* 65±4 (44)* 67±5 (49)* 50ng)

*Statistically significant

Table 5: Influence of TER199 on colony formation by normal human bone marrow GM-progenitor cells stimulated by ***combinations*** of cytokines.

L18 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD Properties and Distribution of GST Isoenzymes

The various GST isoenzymes are dimeric proteins formed

by binary ***combinations*** of monomers encoded by at least fifteen known genes in four gene families, resulting in the theoretical possibility of several dozen different. . .

availability of a substantial family of isoenzymes which is unevenly distributed as to its members with respect to normal and tumor tissue, ***combined*** with differences between the family members in substrate specificity and inhibitor sensitivity, makes this family an important target for designing therapies for conditions. . .

Figures 3a and 3b are graphs showing the decomposition of ***TER*** ***286*** and TER 322 by various GSTs.

Figure 5 shows the effect of ***TER*** ***286*** on growth of tumors in mice.

Figure 6 shows the effect of 100-200 mg/kg ***TER*** ***286*** on the GM-CFU in bone marrow of mice.

Figure 7 shows the dose-dependence of bone marrow GM-CFU for administration of ***TER*** ***286*** .

Modes of Carrying Out the Invention

The compounds of Formula (1) are prodrugs which can be used selectively to target tissues having. . . specificity to the prodrug provided. As shown below, the prodrugs prepared for illustration, TER 230, as a model compound, and TER 231, ***TER*** ***286*** , TER 296 and TER 303 as effective prodrugs, are differentially activated by GST enzymes of the A, 7 and a classes. These. . .

T-Glutamyl-a-Amino-o-((2-ethyl-N,N,N,N-tetra(2'-chloro)ethylphosphoramidate)sulfonyl)propionylglycine, (TER 231);

is

T-Glutamyl-a-Amino-o-((2-ethyl-N,N,N,N-tetra(21-chloro)ethylphosphoramidate)sulfonyl)propionyl-(R)-(-)-phenylglycine (***TER*** ***286***);

T-Glutamyl-a-Amino-fl-((2-ethyl-N,N,N,N-tetra(21-chloro)ethylphosphoramidate)sulfonyl)propionyl-phenylalanine (TER 303);

7-Glutamyl-a-amino-O-(i-phenyl, 2-ethyl-N,N,N,N-tetra(21-chloroethyl)phosphoramidate)sulfonyl)propionyl glycine (TER 296);

T-Glutamyl-a-amino-fl-(i-phenyl, 2-ethyl-N,N,N,N-tetra(21-chloroethyl)phosphoramidate)sulfonyl)propionyl (R)-(-)-phenylglycine (TER 297);

T-Glutamyl-u-amino-fl(2-ethyl, N,N-bis(2'-chloroethyl)carbamoyl)sulfonyl)propionyl glycine (TER 322) and its diethyl ester (TER 325); and

T-Glutamyl-u-amino-fl-((2-ethyl-(4-benzyloxy(N,N,N',N'tetrakis(2-chloroethyl)phosphorodiamidate))carbamido)sulfonyl)propionyl glycine.

base or

acid at a temperature of from about 0°C to about 100°C, preferably at room temperature either in water alone or in ***combination*** with an inert water-miscible organic solvent such as methanol, ethanol or dioxane.

the

compounds exemplified below, TER 231 is especially susceptible to cleavage by GST M1a-1a; TER 303 is especially susceptible to cleavage by A1-1; ***TER*** ***286*** is particularly susceptible to cleavage by P1-1 and A1-1, while TER 296 is selectively cleaved by P1. Thus, in treating a tumor. . . tumor, they appear to stimulate GM progenitors in bone marrow. There is relatively little organ toxicity and no evidence of leukocytosis. For ***TER*** ***286*** , the relevant isoenzyme, GST P1-1 is elevated in more than

75% of human tumor specimens from breast, lung, liver and colon.

synthesis of TER 296 or TER

297, α -amino- β -sulfhydryl phenylpropionic acid is substituted for the cysteine residue in the analog. For the synthesis of

TER ***286*** , phenylglycine is substituted for glycine in the tripeptide as AAc. For synthesis of TER 303, phenyl alanine is substituted for glycine as. . .

a sep. funnel,

and separated. The lower organic layer was saved, and the aqueous layer was extracted with 100 ml of CH₂Cl₂. The ***combined*** organic phases were washed with 500 ml saturated brine and dried over Na₂SO₄. The solution was filtered and reduced to an oil under. . .

to separate. The lower organic layer was removed and

saved, and the upper layer was extracted with 100 ml CH₂Cl₂. The ***combined*** CH₂Cl₂ layers were washed six times with 100 ml portions

- 25

of saturated NaCl and dried over Na₂SO₄. The solution was filtered and. . .

9:1. The reaction was

quenched with dropwise addition of 100 ml water, and extracted twice with 250 ml portions of EtOAc. The ***combined*** organic extracts were washed twice with 100 ml portions of brine and dried over Na₂SO₄. This was filtered and evaporated to 8.3. . .

stirred overnight. The mixture was poured into

35 ml of water and extracted with two 50 ml portions of toluene, and the ***combined*** organic phases were dried over Na₂SO₄ and concentrated to a viscous oil. TLC (9:1 EtOAc:MeOH) showed one spot, rf 0 UV active.. . .

T-Glutamyl-u-Amino-o-((2-ethyl,-N,N,N,N-tetra(21-chloro). ethylphosphoramidate)sulfonyl)propionyl-(R)-(-)-phenylglycine (***TER*** ***286***);

T-Glutamyl-u-Amino-o-((2-ethyl-N,N,N,N-tetra(2'-chloro)ethylphosphoramidate)sulfonyl)propionyl-phenylalanine (TER 303);

T-Glutamyl-u-Amino-O-(1-phenyl, (2-ethyl-N,N,N,N-tetra(2-chloro)ethylphosphoramidate)sulfonyl) propionyl glycine (TER 296);

T-Glutamyl-u-Amino (1-phenyl, (2-ethyl-N,N,N,N-tetra(21-chloro)ethylphosphoramidate)sulfonyl) propionyl (R)-(-)-phenylglycine (TER 297).

Further details with respect to ***TER*** ***286*** are as follows.

TER ***286*** was similarly tested with the results shown in

Figure 3a. Both PI-I and AI-I accelerate the cleavage of ***TER*** ***286*** roughly six times faster than background; there is negligible acceleration of cleavage with Mla-Ia.

prodrug

selected, specificity can be obtained for any of the three human GSTs tested. Thus, TER 29G is selectively cleaved by Pi-1; ***TER*** ***286*** is selectively cleaved by PI-1 and AI-1; TER 303 is selectively cleaved by AI-1; and TER 231 by Mla-Ia.

when

MCF-7 tumor cells transfected by P1-1 were compared to cells transfected only with the control vector. As shown in Figure 4a, when ***TER*** ***286*** is employed, cells containing high P1-1 enzyme levels are sensitized 4-fold to the prodrug compared to controls; Figure 4b shows a 2-fold. . .

were obtained for MCF-7 cells which

are sensitive to CTX as compared to CTX-resistant forms. The CTX-resistant cells were more sensitive to ***TER*** ***286*** by a factor of 1.8 as compared to cells sensitive to CTX in a standard clonogenic assay.

In Figure 5, the squares represent controls; circles represent 300 mg/kg of ***TER*** ***286*** ; triangles represent 400 mg/kg of the same drug. The points shown are the mean + SEM of 5-7 mice per group.

Example 6

Effect of Prodrug on Bone Marrow

In the assay, B6D2F1 mice were treated with various doses of ***TER*** ***286*** intraperitoneally either as a single injection or as five daily injections. Femoral bone marrows were harvested 24 hours later and assayed for. . . results are shown in Figure 6. Increases up to 1800i of controls for GM-CFU were obtained with administration of 100-200 mg/kg of ***TER*** ***286*** ; the values shown are the mean plus SD of 2-3 experiments.

Further, as shown in Figure 7, the optimum dosage range appears to be in this region of 100-200 mg/kg for ***TER*** ***286*** .

L18 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD Properties and Distribution of GST Isoenzymes

The various GST isoenzymes are dimeric proteins formed by binary ***combinations*** of monomers encoded by at least fifteen known genes in four gene families, resulting in the theoretical possibility of several dozen different. . .

availability of a substantial family of isoenzymes which is unevenly distributed as to its members with respect to normal and tumor tissue, ***combined*** with differences between the family members in substrate specificity and inhibitor sensitivity, makes this family an important target for designing therapies for conditions. . .

2 is a graph showing the decomposition of TER 231 by various GSTs,

Figure 3 is a graph showing the decomposition of ***TER*** ***286*** by various GSTs.

for various chemotherapeutic agents with respect to cells having high or low levels of GST P1

Figure 5 shows the effect of ***TER*** ***286*** on growth of tumors in mice.

Figure 6 shows the effect of 100-200 mg/kg ***TER*** ***286*** on the GM-CFU in bone marrow of mice.

Figure 7 shows the dose-dependence of bone marrow GM-CFU for administration of ***TER*** ***286*** .

Modes of Carrying Out the Inventio

The compounds of Formula (1) are prodrugs which can be used selectively to target tissues having. . . specificity to the prodrug provided. As shown below, the prodrugs prepared for illustration, TER 230, as a model compound, and TER 231, ***TER*** ***286*** , TER 296 and TER 303 as effective prodrugs, are differentially activated by GST enzymes of the A, w and a classes. These. . .

T-Glutamyl-a-Amino-fl-((2-ethyl-N,N,N,N-tetra(21-chloro)ethylphosphoramidate)sulfonyl)propionylglycine, (TER 231)1

7-Glutamyl-a-Amino-O-((2-ethyl-N,N,N,N-tetra(21-chloro)ethylphosphoramidate)sulfonyl)propionyl-(R)-(-)-phenylglycine (***TER*** ***286***);

- 13 -

oy-Glutamyl-oi-Amino-O-((2-ethyl-N,N,N,N-tetra(21-chloro)ethylphosphoramidate)sulfonyl)propionyl-phenylalanine (TER 303);

T-Glutamyl-a-Amino-fl-(l-phenyl, 2-ethyl-N,N,N,N-tetra(21-chloro)ethylphosphoramidate)sulfonyl)propionyl glycine (TER 296);

7-Glutamyl-u-Amino-fl-(1-phenyl, 2-ethyl-N,N,N,N-tetra(21-chloro)ethylphosphoramidate)sulfonyl)propionyl (R)-(-)-phenylglycine (TER 297).

base or

acid at a temperature of from about 0°C to about 100°C, preferably at room temperature either in water alone or in

combination with an inert water-miscible organic solvent such as methanol, ethanol or dioxane.

exemplified below, TER 231 is especially susceptible

to cleavage by GST M1a-1a; TER 303 is especially susceptible to cleavage by A1-1; ***TER*** ***286*** is particularly susceptible to

cleavage by P1-1 and A1-1, while TER 296 is selectively cleaved by P1. Thus, in treating a tumor. . . tumor, they appear to

stimulate GM progenitors in bone marrow, There is relatively little organ toxicity and no evidence of leukocytosis, For ***TER*** ***286***, the relevant isoenzyme, GST P1-1 is elevated in more than 75% of human tumor specimens from breast, lung, liver and colon.

for synthesis of TER 296 or TER

297, a-amino-o-sulphydryl-o-phenylpropionic acid is substituted for the cysteine residue in the analog. For the synthesis of

TER ***286***, phenylglycine is substituted for glycine in the tripeptide as AAC. For synthesis of TER 303, phenyl alanine is substituted for glycine as. . .

sep. funnel,

and separated. The lower organic layer was saved, and the aqueous layer was extracted with 100 ml of CH₂Cl₂. The ***combined*** organic phases were washed with 500 ml saturated brine and dried over Na₂SO₄. The solution was filtered and reduced to an oil under. . .

to separate. The lower organic layer was removed and

35 saved, and the upper layer was extracted with 100 ml CH₂Cl₂. The ***combined*** CH₂Cl₂ layers were washed six times with 100 ml portions

- 23

of saturated NaCl, and dried over Na₂SO₄- The solution was filtered. . .

9:1. The reaction was

quenched with dropwise addition of 100 ml water, and extracted twice with 250 ml portions of EtOAc. The ***combined*** organic extracts were washed twice with 100 ml portions of brine and dried over Na₂SO₄. This was filtered and evaporated to 8.3. . .

stirred overnight. The mixture was poured into

35 ml of water and extracted with two 50 ml portions of toluene, and the ***combined*** organic phases were dried over Na₂SO₄ and concentrated to a viscous oil. TLC (9:1 EtOAc:MeOH) showed one spot, R_f 0.7, UV active.. . .

7-Glutamyl-u-Amino-g-((2-ethyl-N,N,N,N-tetra(21-chloro)ethylphosphoramidate)sulfonyl)propionyl-(R)-(-)-phenylglycine (***TER*** ***286***);

7-Glutamyl-a-Amino-fl-((2-ethyl-N,N,N,N-tetra(21-chloro)ethylphosphoramidate)sulfonyl)propionyl-phenylalanine (TER 303);

7-Glutamyl-a-Amino (1-phenyl, (2-ethyl-N,N,N,N-

tetra(21-chloro)ethylphosphoramidate)sulfonyl) propionyl glycine (TER 296);
7-Glutamyl-a-Amino-fl-(l-phenyl, (2-ethyl-N,N,N,N-tetra(21-chloro)ethylphosphoramidate)sulfonyl) propionyl (R)-(-)-phenylglycine (TER 297).

Further details with respect to ***TER*** ***286*** may be found in Lyttle, M.H. et al. J Med Chem (1994) 37:1501-1507; Lyttle, M. et al, J Med Chem (1994) 34:189. . . .

TER ***286*** was similarly tested with the results shown in Figure 3. Both PI-1 and AI-I accelerate the cleavage of ***TER*** ***286*** roughly six times faster than background; there is negligible acceleration of cleavage with Mla-la.

when MCF-7 tumor cells transfected by PI-1 were compared to cells transfected only with the control vector. As shown in Figure 4a, when ***TER*** ***286*** is employed, cells containing high P1-1 enzyme levels are sensitized 4-fold to the prodrug compared to controls; Figure 4b shows a 2-fold. . . .

obtained for MCF-7 cells which are sensitive to CTX as compared to CTX-resistant forms. The 25 CTX-resistant cells were more sensitive to ***TER*** ***286*** by a factor of 1,8 as compared to cells sensitive to CTX in a standard clonogenic assay.

- 33 -

In Figure 5, the squares represent controls; circles represent 300 mg/kg of- ***TER*** ***286*** ; triangles represent 400 mg/kg of the same drug. The points shown are the mean ± SEM of 5-7 mice per group.

Example 6

Effect of Prodrug on Bone Marrow

In the assay, B6D2F₁ mice were treated with various doses of ***TER*** ***286*** intraperitoneally either as a single injection or as five daily injections. Femoral bone marrows were harvested 24 hours later and assayed for. . . . results are shown in Figure 6, Increases up to 18016 of controls for GM-CPU were obtained with administration of 100-200 mg/kg of ***TER*** ***286*** ; the values shown are the mean plus SD of 2-3 experiments.

Further, as shown in Figure 7, the optimum dosage range appears to be in this region of 100-200 mg/kg for ***TER*** ***286*** .

=> s cancer? or tumor? or neoplas?

80405 CANCER?

67062 TUMOR?

23301 NEOPLAS?

L19 100034 CANCER? OR TUMOR? OR NEOPLAS?

=> s l19/clm

23115 CANCER?/CLM

15601 TUMOR?/CLM

3791 NEOPLAS?/CLM

L20 32848 (CANCER?/CLM OR TUMOR?/CLM OR NEOPLAS?/CLM)

=> s l20 and l18

L21 2 L20 AND L18

=> d ibib 1-2

L21 ANSWER 1 OF 2 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999037802 PCTFULL ED 20020515 <<LOGINID::2006C
TITLE (ENGLISH): METHODS TO IDENTIFY MYELOSTIMULANTS
TITLE (FRENCH): METHODES D'IDENTIFICATION DE MYELOSTIMULANTS
INVENTOR(S): KAUVAR, Lawrence, M.
PATENT ASSIGNEE(S): TELIK, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
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WO 9937802	A1	19990729
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DESIGNATED STATES

W: AU CA GD IN JP AT BE CH CY DE DK ES FI FR GB GR IE IT
LU MC NL PT SE

APPLICATION INFO.: WO 1999-US765 A 19990114

PRIORITY INFO.: US 1998-09/010,390 19980121

L21 ANSWER 2 OF 2 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995009865 PCTFULL ED 20020514 <<LOGINID::2006C
TITLE (ENGLISH): GLUTATHIONE S-TRANSFERASE-ACTIVATED COMPOUND
TITLE (FRENCH): COMPOSES ACTIVES PAR LA GLUTATHIONE S-TRANSFEE
INVENTOR(S): KAUVAR, Lawrence, M.;
LYTTLE, Matthew, H.;
SATYAM, Apparao
PATENT ASSIGNEE(S): TERRAPIN TECHNOLOGIES, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
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WO 9509865	A1	19950413
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DESIGNATED STATES

W: AU CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT
SE

APPLICATION INFO.: WO 1994-US10796 A 19940923

PRIORITY INFO.: US 1993-8/130,736 19931001

US 1994-8/130,736 19940919

=> s l19 and l8

'RN' IS NOT A VALID FIELD CODE

452833 COMBINATION

199923 COMBINATIONS

492208 COMBINATION

(COMBINATION OR COMBINATIONS)

0 439943-59-6/RN

429338 PY>2002

L22 0 L19 AND L8

=> s l19 and l18

L23 5 L19 AND L18

=> d kwic 3

L23 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . effects

can be neutropenia, thrombocytopenia and immune suppression generally. These side effects are not only unpleasant, but they also restrict the efficacy of ***cancer*** therapy and place the subject at serious risk of infection and uncontrolled bleeding.

Disclosure of the Invention

The invention provides compounds which are useful in modulating hematopoiesis generally and as aids to chemotherapeutic treatment of ***tumors*** by virtue of their ability to exert a protective effect on the hematopoietic system with respect to toxic agents which are otherwise useful. . . .

cell populations in the course of bone marrow transplantation. The invention is

further directed to the use of compounds of the invention as ***tumor*** -specific chemo- or radiosensitizers, thus potentiating the effect of treatment, and as generalized chemoprotectants, The invention also includes pharmaceutical compositions containing the compounds of the. . .

Brief Description of the Drawings

Figure 1a shows the effect of TER199 on the survival of ***tumor*** cells treated with various concentrations of chlorambucil.

toxic effect of TER199 in contrast to its unesterified form on HT4-1 cells, Figure 2 is a graph showing the effect of various ***combinations*** of chlorambucil either alone or in ***combination*** with ethacrynic acid or TER199.

chemotherapeutic agents, Second, they usually inhibit at least one class of the GST isoenzymes, including the n subclass, which is particularly prevalent in ***tumor*** cells. Third, the compounds of formula (1) directly potentiate the effect of chemotherapeutic agents in the destruction of ***tumor*** cells. This ***combination*** of qualities makes the compounds of the invention useful both as hematopoiesis potentiating agents directly and to ameliorate the negative effects of chemotherapeutic. . .

Example 1

Use of the Compounds of the Invention in Potentiation of Cytotoxic Agents in Human Cells

This example describes: 1) potentiation in human ***tumor*** cells of a cytotoxic agent currently used in ***cancer***

chemotherapy by GST inhibitors, including compounds of the present invention, as well as 2) enhanced intracellular efficacy of esterified forms of these compounds,

HT-29 (human colon adenocarcinoma) cells were obtained from Dr. Roberto Ceriani (***Cancer*** Research Fund of Contra Costa County, Walnut Creek, CA) and were used in log phase of growth unless otherwise specified.

The results in Tables 1-3 show that several GSH analogs found to be inhibitors of GSH also potentiate killing of human ***tumor*** cells in culture by CMB which is a substrate for various GSTs. Results of potentiation tests with several GST inhibitors in HT29. . .

CMB, reducing the concentration CMB needed for 50% cell killing by a DMF of 1,08, In contrast the diethyl ester of 7E-C(Bz)-qG (***TER*** ***199***) at only 12.5 pM enhanced CMB cytotoxicity by a factor of 1

Preferential expression of GST isoenzyme P1-1 has been reported in a range of human ***tumors*** . In the present study the efficacy of CMB potentiation of the several GST inhibitors tested correlated directly with their

- 18 -

potencies as. . .

Example 2

Potentiation of Melphalan Toxicity in vivo

Male scid mice were subcutaneously implanted with HT4-1 ***tumors*** from donor mice. HT4-1 is a subclone of HT-29, a human colon ***cancer*** . When ***tumors*** reached approximately 100 MM3, the mice were randomized into six treatment groups and treated for seven days as follows.

The mice were monitored for weight changes and ***tumor*** volumes were determined by measurement with calipers.

The ***tumor*** growth was monitored until the average ***tumor***

size reached 1500 MM3 for all groups except melphalan with ethacrynic acid. This group failed to reach this volume even after 72 days.

The results were computed in terms of the ***tumor*** volume in the drug treated mice as a percentage of control ***tumor*** volume (i.e., in the group administered vehicle alone). In group 11 administered melphalan alone, the ***tumors*** were approximately 75% of the volume of controls. In group 5 when TER199 was administered along with the melphalan, the ***tumor*** volume mean was approximately 55% of control. For group 4 administered a ***combination*** of melphalan and ethacrynic acid, the volumes were approximately 35% of control. Thus, both ethacrynic acid and TER199 potentiate the effects of melphalan, (The volume measurements were taken at the time control ***tumors*** reached 1500 nun3

Example 3

Metabolic Effects of the Invention Compounds

The metabolic effects related to toxicity of the compounds of the invention on. . .

PG intraperitoneally. Femoral bone marrows were harvested 24 hours later and assayed for GM-CFU by the method of East, C.J. et. al. ***Cancer*** Chemother Pharmacol (1992) 31:123 An increase in the number of colonies in a dose-dependent manner up to a dosage of 90 mg/kg. . .

GM-CSFI G-CSFI M-CSFI Flt3/Flk-2 and Steel factor (stem cell factor/c-kit ligand). Of particular interest was the finding that TER199 enhances colony formation stimulated by ***combinations*** of cytokines. Additionally, the enhancing effect is more pronounced in human than in murine bone marrow, These results suggest that TER199 has. . .

(60)* 65±4 (44)* 67±5 (49)* 50ng)

'Statistically significant

Table 5: Influence of TER199 on colony formation by normal human bone marrow GM-progenitor cells stimulated by ***combinations*** of cytokines.

=>

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E2	1	TER 183/CN
E3	1	--> TER 199/CN
E4	1	TER 200/CN
E5	1	TER 206/CN
E6	1	TER 211/CN
E7	1	TER 230/CN
E8	1	TER 231/CN
E9	1	TER 286/CN
E10	1	TER 317/CN
E11	1	TER 322/CN
E12	1	TER 324/CN
E13	1	TER 338/CN
E14	1	TER 3938/CN
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E21	5	TER(5,6)FULLERENE-C50-D5H(6)/CN
E22	3	TER(5,6)FULLERENE-C50-D5H(6), DOCOSAHYDRO-/CN
E23	2	TER(5,6)FULLERENE-C50-D5H(6), OCTADECALHYDRO-/CN
E24	1	TER-1H-INDOLE, 2,2',2'',3,3',3''-HEXAPHENYL-/CN
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L1 1 "TER 199"/CN

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L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN

RN 168682-53-9 REGISTRY

CN Glycine, L-.gamma.-glutamyl-S-(phenylmethyl)-L-cysteinyl-2-phenyl-,
diethyl ester, (2R)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Glycine, N-[N-L-.gamma.-glutamyl-S-(phenylmethyl)-L-cysteinyl]-D-2-phenyl-,
diethyl ester

OTHER NAMES:

CN ***Ter 199***

CN Terrapin 199

CN TLK 199

FS STEREOSEARCH

MF C27 H35 N3 O6 S

CI COM

SR CA

LC STN Files: ADISINSIGHT, BIOSIS, CA, CAPLUS, DDFU, DRUGU, IMSDRUGNE
IMSPATENTS, IMSRESEARCH, PHAR, PROUSDDR, TOXCENTER, USPAT2, U:

DT.CA Caplus document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES
(Uses)

RL.NP Roles from non-patents: BIOL (Biological study); USES (Uses)

Absolute stereochemistry.

/ Structure 2 in file .gra /

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